

WHAT IS CLAIMED IS:

1. A method of creating a chemical compound library comprising:
selecting compounds having a molecular weight of no greater
than about 350 grams/mole; and
selecting compounds having a solubility in deuterated water of at
least about 1 mM at room temperature.
2. The method of claim 1 wherein a majority of the compounds in the
chemical compound library have a molecular weight of no greater than
about 350 grams/mole and a solubility in deuterated water of at least
about 1 mM at room temperature.
3. The method of claim 2 wherein all of the compounds in the chemical
compound library have a molecular weight of no greater than about 350
grams/mole and a solubility in deuterated water of at least about 1 mM at
room temperature.
4. The method of claim 1 wherein the compounds selected have a molecular
weight of no greater than about 325 grams/mole.
5. The method of claim 4 wherein the compounds selected have a molecular
weight of less than about 325 grams/mole.
6. A chemical compound library comprising compounds having a molecular
weight of no greater than about 350 grams/mole and a solubility in
deuterated water of at least about 1 mM at room temperature.
7. The library of claim 6 wherein a majority of the compounds have a
molecular weight of no greater than about 350 grams/mole and a
solubility in deuterated water of at least about 1 mM at room temperature.
8. The library of claim 7 wherein all of the compounds have a molecular

weight of no greater than about 350 grams/mole and a solubility in deuterated water of at least about 1 mM at room temperature.

9. The library of claim 6 wherein the compounds have a molecular weight of no greater than about 325 grams/mole.
10. The library of claim 9 wherein the compounds have a molecular weight of less than about 325 grams/mole.
11. A method of identifying a lead chemical template, the method comprising:
selecting compounds having a molecular weight of no greater than about 350 grams/mole and a solubility in deuterated water of at least about 1 mM at room temperature to create a chemical compound library;
identifying at least one compound from the library that functions as a ligand to a target molecule having a dissociation constant of at least about 100 μ M; and
using the ligand to identify a lead chemical template.
12. The method of claim 11 wherein a majority of the compounds in the chemical compound library have a molecular weight of no greater than about 350 grams/mole and a solubility in deuterated water of at least about 1 mM at room temperature.
13. The method of claim 12 wherein all of the compounds in the chemical compound library have a molecular weight of no greater than about 350 grams/mole and a solubility in deuterated water of at least about 1 mM at room temperature.
14. The method of claim 11 wherein the compounds selected for the library have a molecular weight of no greater than about 325 grams/mole.
15. The method of claim 14 wherein the compounds selected for the library

have a molecular weight of less than about 325 grams/mole.

16. The method of claim 11 wherein the dissociation constant of a lead chemical template to the target molecule is at least about 1 μ M.

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17. The method of claim 11 wherein the target molecule is a protein.

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18. A method of identifying a compound that binds to a target molecule, the method comprising:

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providing a plurality of mixtures of test compounds, each mixture being in a sample reservoir;

introducing a target molecule into each of the sample reservoirs to provide a plurality of test samples;

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providing a nuclear magnetic resonance spectrometer equipped with a flow-injection probe;

transferring each test sample from the sample reservoir into the flow-injection probe;

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collecting a relaxation-edited nuclear magnetic resonance spectrum on each sample in each reservoir; and

comparing the spectra of each sample to the spectra taken under the same conditions in the absence of the target molecule to identify compounds that bind to the target molecule;

wherein the concentration of target molecule and each compound in each sample is no greater than about 100 μ M.

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19. The method of claim 18 wherein each mixture is in a sample reservoir of a multiwell sample holder.

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20. The method of claim 19 wherein the multiwell sample holder is a 96-well microtiter plate.

21. The method of claim 18 wherein each test compound has a solubility in deuterated water of at least about 1 mM at room temperature.
22. The method of claim 18 wherein each test compound has a molecular weight of no greater than about 350 grams/mole.
23. The method of claim 18 wherein collecting a relaxation-edited nuclear magnetic resonance spectrum comprises collecting a 1D relaxation-edited nuclear magnetic resonance spectrum.
24. The method of claim 23 wherein collecting a 1D relaxation-edited nuclear magnetic resonance spectrum comprises collecting a 1D relaxation-edited ¹H nuclear magnetic resonance spectrum.
25. The method of claim 18 wherein the mixture of compounds comprises at least about 3 compounds, each having at least one distinguishable resonance in a 1D NMR spectrum of the mixture.
26. The method of claim 25 wherein the mixture of compounds comprises at least about 6 compounds.
27. The method of claim 25 wherein the ratio of target molecule to each test compound in each sample reservoir is about 1:1.
28. The method of claim 18 wherein the concentration of target molecule and each compound in each sample is no greater than about 50 μM.
29. The method of claim 18 wherein the dissociation constant of a compound that binds to the target molecule is at least about 100 μM.
30. The method of claim 18 wherein the target molecule is a protein.
31. A method of identifying a compound that binds to a target molecule, the

method comprising:

providing a plurality of mixtures of test compounds, each mixture being in a sample reservoir;

5 introducing a target molecule into each of the sample reservoirs to provide a plurality of test samples;

providing a nuclear magnetic resonance spectrometer equipped with a flow-injection probe;

transferring each test sample from the sample reservoir into the flow-injection probe;

10 collecting a WaterLOGSY nuclear magnetic resonance spectrum on each sample in each reservoir; and

analyzing the spectra of each sample to distinguish binding compounds from nonbinding compounds by virtue of the opposite sign of their water-ligand NOEs.

15 32. The method of claim 31 wherein the concentration of target molecule is no greater than about 10 μM .

33. The method of claim 32 wherein the concentration of target molecule is
20 no greater than about 1 μM .

34. The method of claim 31 wherein the concentration of each compound in each sample is no greater than about 100 μM .

25 35. The method of claim 31 wherein each test compound has a solubility in deuterated water of at least about 1 mM at room temperature.

36. The method of claim 31 wherein each mixture is in a sample reservoir of a multiwell sample holder.

30 37. The method of claim 36 wherein the multiwell sample holder is a 96-well microtiter plate.

38. The method of claim 31 wherein each test compound has a molecular weight of no greater than about 350 grams/mole.
- 5 39. The method of claim 38 wherein each test compound has a molecular weight of no greater than about 325 grams/mole.
40. The method of claim 31 wherein collecting a WaterLOGSY nuclear magnetic resonance spectrum comprises collecting a 1D WaterLOGSY nuclear magnetic resonance spectrum.
- 10 41. The method of claim 31 wherein the mixture of compounds comprises at least about 3 compounds, each having at least one distinguishable resonance in a 1D NMR spectrum of the mixture.
- 15 42. The method of claim 41 wherein the mixture of compounds comprises at least about 6 compounds.
43. The method of claim 31 wherein the ratio of target molecule to each test compound in each sample reservoir is about 100:1 to about 10:1.
- 20 44. The method of claim 31 wherein the dissociation constant of a compound that binds to the target molecule is at least about 100 μ M.
- 25 45. The method of claim 31 wherein the target molecule is a protein.
- 30 46. A method of identifying a protein function, the method comprising:
providing a plurality of mixtures of test compounds consisting of known inhibitors, cofactors, and substrates of known proteins, each mixture being in a sample reservoir and containing a plurality of test compounds;
introducing a target molecule into each of the sample reservoirs to provide a plurality of test samples;

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providing a nuclear magnetic resonance spectrometer equipped
with a flow-injection probe;

transferring each test sample from the sample reservoir into the
flow-injection probe;

5 collecting a WaterLOGSY nuclear magnetic resonance spectrum
on each sample in each reservoir;

10 comparing the spectra of each sample to the spectra taken under
the same conditions in the absence of the target molecule to identify
compounds that bind to the target molecule, wherein the concentration of
target molecule and each compound in each sample is no greater than
about 5 μM and 125 μM , respectively; and

determining a function of the target molecule based upon the test
compounds that bind to the target molecule.

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